

WHAT IS CLAIMED IS:

1. (Withdrawn) An antibody or an antibody fragment, comprising an antigen recognition region capable of binding a metal ion and a chelator thereof, wherein the antibody or the antibody fragment is capable of inhibiting an activity of a metalloprotein.
2. (Withdrawn) The antibody or antibody fragment of claim 1, wherein said metal ion is a transition metal ion selected from the group consisting of Vanadium, Selenium, Molybdenum, Cobalt, Zinc, Copper, Iron, Gallium, Bismuth, Aluminum, Gold, Platinum, Manganese, Chromium, Silver, Antimony, Thallium, Cadmium, Nickel, Mercury and Lead.
3. (Withdrawn) The antibody or antibody fragment of claim 1, wherein said chelator is a polyamine.
4. (Withdrawn) The antibody or antibody fragment of claim 3, wherein said polyamine is at least two histidine molecules.
5. (Withdrawn) The antibody or antibody fragment of claim 3, wherein said polyamine is selected from the group consisting of ethylene diamine, cyclam, porphyrin, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanolamine, aminoethylpiperazine, pentaethylenhexamine, captopril, penicilamine, N,N'-bis(3-aminopropyl)-1,3-propanediamine, N,N'-Bis-(2-aminoethyl)-1,3-propanediamine, 1,7-dioxo-4,10-diazacyclododecane, 1,4,8,11-tetraaza cyclotetradecane-5,7-dione, 1,4,7-triazacyclononane, 1-oxa-4,7,10-triazacyclododecane, 1,4,8,12-tetraazacyclopentadecane, and 1,4,7,10-tetraazacyclododecane.
6. (Withdrawn) The antibody or antibody fragment of claim 1, wherein said metalloprotein is selected from the group consisting of neutrophil collagenase, collagenase-3, gelatinase A, gelatinase B, stromelysins-2 and 3, matrilysin, macrophage elastase; membrane-type MMPs, aggrecanase, tumor necrosis factor converting enzyme, cytokine convertases, adhesion molecule shedding enzymes, endothelin converting enzyme, angiotensin converting enzyme, neutral endopeptidase, FTSH - bacterial metalloprotease, metallo-lactamase (carbapenases), bacterial toxins and ras farnesyl protein transferase and carbonic anhydrase.
7. (Currently Amended) A method of producing a metalloprotein inhibitor,
the method comprising:

- (a) generating antibodies directed at a composition including a metal ion-bound chelator, wherein said composition is selected having structural and electronic properties similar to a functional domain of the metalloprotein, thereby producing the metalloprotein inhibitor; and
 (b) testing an inhibitory effect of said antibodies on the metalloprotein, thereby producing the metalloprotein inhibitor

8. (Original) The method of claim 7, wherein said antibodies are polyclonal antibodies.

9. (Original) The method of claim 7, wherein said antibodies are monoclonal antibodies.

10. (Original) The method of claim 7, wherein said metal ion is a transition metal ion selected from the group consisting of Vanadium, Selenium, Molybdenum, Cobalt, Zinc, Copper, Iron, Gallium, Bismuth, Aluminum, Gold, Platinum, Manganese, Chromium, Silver, Antimony, Thallium, Cadmium, Nickel, Mercury and Lead.

11. (Original) The method of claim 7, wherein said chelator is a polyamine.

12. (Original) The method of claim 11, wherein said polyamine is at least two histidine molecules.

13. (Original) The method of claim 11, wherein said polyamine is selected from the group consisting of ethylene diamine, cyclam, porphyrin, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanolamine, aminoethylpiperazine, pentaethylenhexamine, captopril, penicillamine, N,N'-bis(3-aminopropyl)-1,3-propanediamine, N,N'-Bis-(2-aminoethyl)-1,3-propanediamine, 1,7-dioxo-4,10-diazacyclododecane, 1,4,8,11-tetraaza cyclotetradecane-5,7-dione, 1,4,7-triazacyclononane, 1-oxa-4,7,10-triazacyclododecane, 1,4,8,12-tetraazacyclopentadecane, and 1,4,7,10-tetraazacyclododecane.

14. (Original) The method of claim 7, wherein said composition is selected from the group consisting of tetra-carboxy phenyl porphyrin Co(II), tetra-carboxy phenyl porphyrin Zn(II), metal-bound aliphatic amino group containing compound, metal-bound alicyclic amino group containing compound and metal-bound peptides.

15. (Withdrawn) An antibody or an antibody fragment, comprising an antigen recognition region capable of binding a metal ion and a chelator thereof, wherein the antibody or the antibody fragment is capable of inhibiting an activity of a matrix metalloprotease.

16. (Withdrawn) The antibody or antibody fragment of claim 15, wherein said metal ion is a transition metal ion selected from the group consisting of Vanadium, Selenium, Molybdenum, Cobalt, Zinc, Copper, Iron, Gallium, Bismuth, Aluminum, Gold, Platinum, Manganese, Chromium, Silver, Antimony, Thallium, Cadmium, Nickel, Mercury and Lead.

17. (Withdrawn) The antibody or antibody fragment of claim 15, wherein said chelator is a polyamine.

18. (Withdrawn) The antibody or antibody fragment of claim 17, wherein said polyamine is at least two histidine molecules.

19. (Withdrawn) The antibody or antibody fragment of claim 17, wherein said polyamine is selected from the group consisting of ethylene diamine, cyclam, porphyrin, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanolamine, aminoethylpiperazine, pentaethylenhexamine, captopril, penicilamine, N,N'-bis(3-aminopropyl)-1,3-propanediamine, N,N'-Bis-(2-aminoethyl)-1,3-propanediamine, 1,7-dioxo-4,10-diazacyclododecane, 1,4,8,11-tetraaza cyclotetradecane-5,7-dione, 1,4,7-triazacyclononane, 1-oxa-4,7,10-triazacyclododecane, 1,4,8,12-tetraazacyclopentadecane, and 1,4,7,10-tetraazacyclododecane.

20. (Withdrawn) A pharmaceutical composition comprising an antibody or an antibody fragment including an antigen recognition region capable of binding a metal ion and a chelator thereof and a physiologically acceptable carrier, wherein said antibody or antibody fragment is capable of inhibiting an activity of a matrix metalloprotease.

21. (Withdrawn) The pharmaceutical composition of claim 20, wherein said antibody is a polyclonal antibody.

22. (Withdrawn) The pharmaceutical composition of claim 20, wherein said antibody is a monoclonal antibody.

23. (Withdrawn) The pharmaceutical composition of claim 20, wherein said metal ion is a transition metal ion selected from the group consisting of Vanadium, Selenium, Molybdenum, Cobalt, Zinc, Copper, Iron, Gallium, Bismuth, Aluminum, Gold, Platinum, Manganese, Chromium, Silver, Antimony, Thallium, Cadmium, Nickel, Mercury and Lead.

24. (Withdrawn) The pharmaceutical composition of claim 20, wherein said chelator is a polyamine.

25. (Withdrawn) The pharmaceutical composition of claim 24, wherein said polyamine is at least two histidine molecules.

26. (Withdrawn) The pharmaceutical composition of claim 24, wherein said polyamine is selected from the group consisting of ethylene diamine, cyclam, porphyrin, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanolamine, aminoethylpiperazine, pentaethylenhexamine, captopril, penicilamine, N,N'-bis(3-aminopropyl)-1,3-propanediamine, N,N'-Bis-(2-aminoethyl)-1,3-propanediamine, 1,7-dioxo-4,10-diazacyclododecane, 1,4,8,11-tetraaza cyclotetradecane-5,7-dione, 1,4,7-triazacyclononane, 1-oxa-4,7,10-triazacyclododecane, 1,4,8,12-tetraazacyclopentadecane, and 1,4,7,10-tetraazacyclododecane.

27. (Withdrawn) The pharmaceutical composition of claim 20, wherein said matrix metalloprotease is selected from the group consisting of MMP-1-MMP23.

28. (Withdrawn) A matrix metalloprotease inhibitor comprising an antibody or an antibody fragment including an antigen recognition region capable of binding a metal ion and a chelator thereof.

29. (Withdrawn) The matrix metalloprotease inhibitor of claim 28, wherein said antibody is a polyclonal antibody.

30. (Withdrawn) The matrix metalloprotease inhibitor of claim 28, wherein said antibody is a monoclonal antibody.

31. (Withdrawn) The matrix metalloprotease inhibitor of claim 28, wherein said metal ion is a transition metal ion selected from the group consisting of Vanadium, Selenium, Molybdenum, Cobalt, Zinc, Copper, Iron, Gallium, Bismuth, Aluminum, Gold,

Platinum, Manganese, Chromium, Silver, Antimony, Thallium, Cadmium, Nickel, Mercury and Lead.

32. (Withdrawn) The matrix metalloprotease inhibitor of claim 28, wherein said chelator is a polyamine.

33. (Withdrawn) The matrix metalloprotease inhibitor of claim 32, wherein said polyamine is at least two histidine molecules.

34. (Withdrawn) The matrix metalloprotease inhibitor of claim 32, wherein said polyamine is selected from the group consisting of ethylene diamine, cyclam, porphyrin, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanolamine, aminoethylpiperazine, pentaethylenhexamine, captopril, penicillamine, N,N'-bis(3-aminopropyl)-1,3-propanediamine, N,N'-Bis-(2-aminoethyl)-1,3-propanediamine, 1,7-dioxo-4,10-diazacyclododecane, 1,4,8,11-tetraaza cyclotetradecane-5,7-dione, 1,4,7-triazacyclononane, 1-oxa-4,7,10-triazacyclododecane, 1,4,8,12-tetraazacyclopentadecane, and 1,4,7,10-tetraazacyclododecane.

35. (Currently amended) ~~A-The method of producing a matrix metalloprotease inhibitor, the method comprising generating antibodies directed at a composition including a metal ion bound chelator, wherein said composition is selected having structural and electronic properties similar to a catalytic domain of the matrix metalloprotease, thereby producing the claim 7, wherein said metalloprotein comprise a matrix metalloprotease inhibitor.~~

36-41. (Cancelled)

42. (Currently amended) The method of claim ~~35~~35, wherein said matrix metalloprotease composition is selected from the group consisting of neutrophil collagenase, collagenase-3, gelatinase A, gelatinase B, stromelysins-2 and 3, matrilysin, macrophage elastase, membrane-type MMPs, aggrecanase, tumor necrosis factor converting enzyme, cytokine convertases, adhesion molecule shedding enzymes, endothelin converting enzyme, angiotensin converting enzyme, neutral endopeptidase, FTSH - bacterial metalloprotease, metallo-lactamase (carbapenases), bacterial toxins and ras farnesyl protein transferase and carbonic anhydrase, tetra-carboxy-phenyl-porphyrin-Co(II), tetra-carboxy-phenyl-porphyrin-Zn(II), metal-bound-aliphatic-amino-group-containing-compound, metal-bound-alkylethio-amino-group-containing-compound and metal-bound-peptides.

43. (Withdrawn) A method of inhibiting matrix metalloprotease activity in a subject in need thereof, the method comprising providing to the subject a therapeutically effective amount of an antibody or an antibody fragment including an antigen recognition region capable of binding a metal ion and a chelator thereof, thereby inhibiting matrix metalloprotease activity in the subject.

44. (Withdrawn) The method of claim 43, wherein said antibody is a polyclonal antibodies.

45. (Withdrawn) The method of claim 43, wherein said antibody is a monoclonal antibodies.

46. (Withdrawn) The method of claim 43, wherein said metal ion is a transition metal ion selected from the group consisting of Vanadium, Selenium, Molybdenum, Cobalt, Zinc, Copper, Iron, Gallium, Bismuth, Aluminum, Gold, Platinum, Manganese, Chromium, Silver, Antimony, Thallium, Cadmium, Nickel, Mercury and Lead.

47. (Withdrawn) The method of claim 43, wherein said chelator is a polyamine.

48. (Withdrawn) The method of claim 47, wherein said polyamine is at least two histidine molecules.

49. (Withdrawn) The method of claim 47, wherein said polyamine is selected from the group consisting of ethylene diamine, cyclam, porphyrin, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanolamine, aminoethylpiperazine, pentaethylenhexamine, captopril, penicillamine, N,N'-bis(3-aminopropyl)-1,3-propanediamine, N,N'-Bis-(2-aminoethyl)-1,3-propanediamine, 1,7-dioxo-4,10-diazacyclododecane, 1,4,8,11-tetraaza cyclotetradecane-5,7-dione, 1,4,7-triazacyclononane, 1-oxa-4,7,10-triazacyclododecane, 1,4,8,12-tetraazacyclopentadecane, and 1,4,7,10-tetraazacyclododecane.

50. (Withdrawn) The method of claim 43, wherein said antibody or said antibody fragment is an active ingredient of a pharmaceutical composition which also includes a physiologically acceptable carrier.

51. (Withdrawn) An article-of-manufacture comprising packaging material and a pharmaceutical composition identified for treating diseases associated with abnormal activity of a matrix metalloprotease being contained within said packaging material, said pharmaceutical composition including, as an active ingredient, an antibody or an antibody fragment including an antigen recognition region capable of binding a metal ion and a chelator thereof, wherein said antibody or antibody fragment is capable of inhibiting an activity of the matrix metalloprotease.

52. (Withdrawn) The article-of-manufacture of claim 51, wherein said metal ion is a transition metal ion selected from the group consisting of Vanadium, Selenium, Molybdenum, Cobalt, Zinc, Copper, Iron, Gallium, Bismuth, Aluminum, Gold, Platinum, Manganese, Chromium, Silver, Antimony, Thallium, Cadmium, Nickel, Mercury and Lead.

53. (Withdrawn) The article-of-manufacture of claim 51, wherein said chelator is a polyamine.

54. (Withdrawn) The article-of-manufacture of claim 53, wherein said polyamine is at least two histidine molecules.

55. (Withdrawn) The article-of-manufacture of claim 53, wherein said polyamine is selected from the group consisting of ethylene diamine, cyclam, porphyrin, diethylenetriamine, triethylenetetramine, triethylenediamine, tetraethylenepentamine, aminoethylethanolamine, aminoethylpiperazine, pentaethylenhexamine, captopril, penicilamine, N,N'-bis(3-aminopropyl)-1,3-propanediamine, N,N'-Bis-(2-aminoethyl)-1,3-propanediamine, 1,7-dioxo-4,10-diazacyclododecane, 1,4,8,11-tetraaza cyclotetradecane-5,7-dione, 1,4,7-triazacyclononane, 1-oxa-4,7,10-triazacyclododecane, 1,4,8,12-tetraazacyclopentadecane, and 1,4,7,10-tetraazacyclododecane.

56. (Withdrawn) A method of qualifying specificity of an antibody to a metal ion and a chelator thereof, the method comprising determining conformational changes in binding of the metal ion to the chelator thereof following binding of the antibody, to thereby qualify the specificity of the antibody to the metal ion and the chelator thereof.

57. (Withdrawn) A method of qualifying specificity of an antibody to a metal ion and a chelator thereof, the method comprising determining electronic changes in the metal ion following binding of the antibody, to thereby qualify the specificity of the antibody to the metal ion and the chelator thereof.